REMARKS

Claim 24 has been canceled without prejudice or disclaimer of subject matter. Accordingly, upon entry of this amendment, claims 1-23 are pending. No new matter is added.

I. Claim Rejections Under 35 USC § 112, Enablement

Claims 1-11 and 16-24 are rejected under 35 U.S.C. § 112, first paragraph, for lack of enablement. The Examiner asserts that the specification, while being enabling for compounds wherein R3 and R4 together form dioxlyl or furanyl, does not reasonably provide enablement for the "broadly" claimed ring structures. According to the Examiner, because various heterocyclic structures may be formed on the core structure of formula I (which are many and have different sizes, polarity, electronegativity and different numbers of heteroatoms), the activity of the compounds of formula I would be questionable. The Examiner further states:

> The predictability in this art is high since a small change in a functional feature could result in a drastic change in activity and such change can also result in an opposite effect or activity. To one of ordinary skill in the art it would be a big job to determine the effect of all the claimed structural changes . . . . it would be a great burden on the Examiner to determine which cancers would be treated with the compounds.

In response, the Applicants respectfully traverse this rejection. The Applicants respectfully note that the Examiner is making an improper utility rejection based on the utility portion of the enablement requirement (since the Examiner asserts that the use or activity of the claimed compounds is "questionable"). Although, a utility rejection can be made under either 35 U.S.C. § 101 or 35 U.S.C. § 112, "to avoid confusion" the MPEP directs that a rejection based on a lack of utility should be made under both statutes. See MPEP § 2107.01(IV), entitled "Relationship Between 35 U.S.C. § 112, First Paragraph, And 35 U.S.C. § 101" ("a rejection based on 'lack of utility,' whether

grounded upon 35 U.S.C. 101 or 35 U.S.C. 112, first paragraph, rests on the same basis [i.e., the asserted utility is not credible]."). Thus, the Applicants will respond as if utility rejection was made under both 35 U.S.C. § 112 and 35 U.S.C. § 101.

A. The Claimed Compounds And Compositions Have Utility

The Examiner is asserting that because the activity, function, or effect of the compounds of formula I is questionable or undetermined, one skilled in the art would not know how to use the invention. In other words, the Examiner is asserting that the use or the utility of the genus of compounds of formula I is questionable and therefore the claims should be rejected. However, this type of analysis and conclusion is strictly forbidden by the law and by the Manual of Patent Examining Procedure (MPEP).

MPEP § 2107.02(III)(A) states that "an applicant's assertion of utility creates a presumption of utility that will be sufficient to satisfy the requirements of 35 U.S.C. 101" as well as the utility requirements of 35 U.S.C. 112. MPEP § 2107.02(III) further states:

> Rejections under 35 U.S.C. 101 [or utility rejections under 35 U.S.C. 112] have been rarely sustained by federal courts . . . in these rare cases, the . . . rejection was sustained either because the applicant failed to disclose any utility for the invention or asserted a utility that could only be true if it violated a scientific principle, such as the second law of thermodynamics, or a law of nature . . . Special care therefore should be taken when assessing the credibility of an asserted . . . utility for a claimed invention. In such cases, a previous lack of success in treating a disease or condition, or the absence of a proven animal model for testing the effectiveness of drugs for treating a disorder in humans, should not, standing alone, serve as a basis for challenging the asserted utility under 35 U.S.C. 101 [or under 35 U.S.C. 112].

In addition, pursuant to MPEP § 2107.01(II), "an invention does not lack utility merely because the particular embodiment disclosed in the patent lacks perfection or performs crudely . . . Nor is it essential that the invention accomplish all its intended functions or operate under all conditions . . . partial success being sufficient to

demonstrate utility . . . In short, the defense of non-utility cannot be sustained without proof of total incapacity."

Moreover, the law and the MPEP clearly forbid utility rejections under 35 U.S.C. 101 and 35 U.S.C. 112 based solely on the unpredictability of extending findings of utility for a species to a genus. *See* MPEP § 2107.03(III) which states that utility found in a species is sufficient to support the utility of the genus; *citing In re Gardner* 475 F.2d 1389 (CCPA 1973), where the court held that the utility for a genus was found to be supported through a showing of a limited number of species. Likewise, according to MPEP § 2107.03(II), structural similarity to a single compound with an established utility supports the utility of structurally similar compounds. *See also John Hopkins University v. Cellpro Inc.*, 152 F.3d 1342 (Fed. Cir. 1998), where a claimed genus of antibodies was found to be enabled and to satisfy the utility requirement based upon the disclosure of only a single species of antibody disclosed in the specification.

Here, the Applicants assert several utilities for the compounds of the present invention in Example 125 (p. 136 of the specification). Thus, this assertion of utility, by itself, creates a presumption of utility that is sufficient to satisfy the utility requirement. Again, please see MPEP § 2107.02(III)(A) which states that "an applicant's assertion of utility creates a presumption of utility that will be sufficient to satisfy the utility requirement."

Furthermore, the Applicants clearly demonstrate that the claimed invention has utility by inhibiting Cdk activity and cell proliferation. See the specification at pp. 136-143, where the Applicants conducted several kinase and cell based assays with 43 different compounds of the present invention. In each case Cdk1 activity was inhibited, Cdk2 activity was inhibited, Cdk4 activity was inhibited, and cell proliferation was inhibited as shown in Table 1 (which summarizes the IC_{50} values). There is absolutely no indication or evidence that other species within the claimed genus (but not included in the above assays would not be useful at some concentration. Again, the Applicants

refer the Examiner to MPEP § 2107.03(III) and *In re Gardner* 475 F.2d 1389 (CCPA 1973), where the court held that the utility for a genus was found to be supported through a showing of a limited number of species; and *John Hopkins University v. Cellpro Inc.*, 152 F.3d 1342 (Fed. Cir. 1998), where a claimed genus of antibodies was found to be enabled and to satisfy the utility requirement based upon the disclosure of only a single species of antibody disclosed in the specification.

Accordingly, the Examiner cannot assert that one skilled in the art would not know how to use the compounds of the genus of formula I in claim 1 solely because the activity of all species in that genus have not been tested. Under the law and MPEP, the utility portion of the enablement requirement is clearly satisfied for the genus and species claimed in the present invention.

B. The Specification Teaches How To Make The Claimed Invention

Furthermore, the specification clearly discloses how to make the compounds of the claimed invention. The specification discloses a variety of synthetic routes for making the compounds of formula I on pages 33-45 of the specification (including ring formation, nucleophilic aromatic substitution, removal of protective groups, isolating stereoisomers, converting compounds of formula I bearing a nitrogen or carboxylic acid group into pharmaceutically acceptable acid addition salts, and converting compounds of formula I bearing a carboxylic acid group into pharmaceutically acceptable esters). Moreover, the specification discloses how to specifically make over 120 species of compounds encompassed by formula I in the examples on pages 49-135 of the specification. Like utility, the "making" portion of the enablement requirement is clearly satisfied for the invention as currently claimed.[1]

[1] Since the Applicants have canceled claim 24 (the method of treatment claim), the only claims remaining are directed to compounds and compositions which are clearly enabled as demonstrated above.

Accordingly, the Applicants respectfully request that the rejection under 35 U.S.C. § 112, first paragraph, for lack of enablement, be withdrawn.

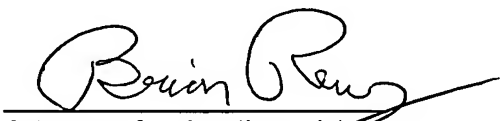
II. Claim Objection

Claims 12-15 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in dependent form including all of the limitations of the base claim and any intervening claims. The Applicants believe that this objection is now moot in view of the above amendment and remarks. Accordingly, the Applicants respectfully request that this objection be withdrawn.

CONCLUSION

No fee is believed to be required in connection with the filing of this Amendment. If any additional fees are deemed necessary, authorization is given to charge the amount of any such fee to Deposit Account No. 08-2525.

Respectfully submitted,



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